Irish Haemochromatosis Association

Carmichael Centre, North Brunswick Street, Dublin 7

Summer/Autumn 2007

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FEATURES

Welcome to the Summer/Autumn Newsletter...

REPORT FROM AGM

The meeting which took place on May 26th was attended by over 80 members. We would like to thank Dr Murphy and the IBTS for generously sponsoring the morning coffee and lunch. Denise McAuliffe from Limerick was elected as a Director of the IHA. Denise is Secretary of the Mid-Western Haemochromatosis Support Group and we are very happy to welcome her on to the board of the IHA. The IHA would like to thank Dr Barry Kelleher, Professor Moira O'Brien and Mr. Paul Nestor for their excellent presentations at the AGM.

Dr. Barry Kelleher's Presentation on Haemochromatosis at 2007 AGM

'Hereditary Haemochromatosis is the most common cause of iron overload. The highest frequency in the world has been identified in Ireland. In this country 1:83 are predisposed to iron overload whereas in the USA the figure given is 1:300. Increasing affluence, longevity and dietary fortification has led to a greater risk of iron overload in those genetically predisposed.

In 2000 the European Association for the study of the Liver (EASL) defined HH as "an inherited disorder resulting from an inborn error of iron metabolism which leads to progressive iron loading of parenchymal cells in the liver, pancreas and heart. In its fully developed stage organ structure and function are impaired".

The first description of the disease was by Trousseau in 1865 and in 1889 the term Haemochromatosis was coined.

Two mutations of the Haemochromatosis gene (HFE) were discovered in 1996 by Feder *et al*, C282Y and H63 D. Iron overload is associated with C282Y homozygosity (C282Y/C282Y) and to a lesser extent with C282Y/ H63 D compound heterozygosity.

Presentation and Symptoms

Fatigue is the most common symptom affecting up to 60% of patients. Other symptoms in the developed syndrome are Arthralgia/ Arthritis, Hepatomegaly/Cirrhosis, Diabetes, cardiac failure and sexual dysfunction.

In general, the severity of the clinical illness is related to the iron burden. The clinical condition evolves in a series of stages beginning with:

1. Clinically insignificant iron overload (0-20 years/0-5g iron storage)
2. Iron overload without disease (approximately 20-40 years/10-20g iron storage)
3. Iron overload with organ damage (greater that 40 years/greater than 20g iron storage)

The outline above suggesting simple step-wise progression of iron overload overlooks the phenotypic

AGM 2007 Photo Gallery

From left to right: Leonora Mullett, Fran Mullaney, Margaret Mullett and Dr Barry Kelleher

Margaret Mullett and Dr Willy Murphy

Brendan Gallagher, Director of IHA

Fran Mullaney, Vice President EFAPH (left) and Professor Moira O'Brien, President of the Irish Osteoporosis Society (right)

variability. Phenotype is the product of interactions between genes and the environment. Not all people with the genetic predisposition will develop significant iron overload. The factors that influence the variability are not completely understood but research is ongoing.

Hepcidin

Hepcidin is a peptide hormone of 25 amino acids produced by the liver. It was first identified in human urine. It is thought to be very important in iron metabolism. Hepcidin deficient mice develop iron overload whereas Hepcidin over-expressors have severe iron deficiency. Mutations in levels of Hepcidin may explain why some people develop more serious disease. (More recent discoveries have shown that Hepcidin directly reacts with ferroportin, a protein that transports iron out of cells that store it.)

"It is important to live life to the full by eating a balanced diet and by avoiding exclusionary iron-free diets."

Diagnosis

The simple blood tests for ferritin and transferrin can be carried out in the doctor's surgery. Ferritin measures the iron in your blood and Transferrin Saturation measures the iron carried in your body. If these tests are above the normal level, a genetic test should be carried out.

Family Screening Recommendations

It is recommended that first degree relatives of confirmed cases of Haemochromatosis as well as children of confirmed case of Haemochromatosis should be screened.

Genetic testing of the spouse: If negative no need to screen the children; if carrier (C282Y or H63D) further genetic testing of children is indicated in those over the age of 20.

Treatment

Phlebotomy is the cornerstone of treatment and has been around since the Middle Ages. It is the removal of blood, similar to blood donation. Each unit of blood (500cc) contains 0.25 grams of iron. Phlebotomy should be carried out weekly until the serum ferritin falls below 50mg/l. Once this goal has been reached, maintenance phlebotomy must be tailored to suit the individual patient by six monthly monitoring of fasting, serum transferrin and serum ferritin. The haemoglobin should be checked before each phlebotomy and phlebotomy deferred if level is <11g/dl.

Prior to the commencement of therapeutic phlebotomy, some patients may require liver biopsy to estimate the degree of fibrosis or cirrhosis.

Who needs a biopsy?

Anyone aged over 40; abnormal liver enzymes; Ferritin over 1000 mg/l need biopsy. Rules are meant for interpretation. Discretion is appropriate in recommending liver biopsy on the basis of age alone.

Other Types of HH

The majority of HH cases are caused by mutations in the HFE gene located on chromosome 6. This disorder is termed type 1 or HFE associated HH.

There are other rare forms of Haemochromatosis not related to the HFE gene. The four main forms are caused by mutations in the genes hemojuvelin, hepcidin, transferrin receptor 2 (TfR2ferroportin) and ferroportin.

Juvenille (JH) or type 2 Haemochromatosis is a more severe form of Haemochromatosis with an earlier age of onset than HFE-HH. Generally patients with JH present with clinical symptoms before 30 years of age and often in teenage years. It is very important to diagnose and treat of an early age.

Dr Kelleher's Take Home Message

In Ireland HH is relatively common, the prognosis is excellent and treatment is relatively straightforward. Ongoing research and new 'molecular' discoveries will help in our continued understanding of this disorder. It is important to live life to the full by eating a balanced diet and by avoiding exclusionary iron-free diets. Remember to be moderate in your alcohol intake and avoid iron and Vitamin C supplements.

Professor Moira O'Brien's Presentation at AGM

Professor O'Brien explained that Osteoporosis is a silent disease and is the commonest bone disease world wide. It can affect all ages and is not just an old ladies disease. It is preventable and treatable. Often the first sign is a fracture (wrist, spine or hip). It occurs in 1 in 3 postmenopausal women and 1 in 5 men. It is a disease characterized by a decrease in bone mass leading to enchanced fragility of the skeleton.

Osteoporosis is present when the bone mineral density is over 2.5 standard deviations below the young adult mean (-2.5 T score). Dexa (Dual energy Xray absorptiometry) is the gold standard to diagnose Osteoporosis. Main cause is gonadal insufficiency which results in low levels of oestrogen in females and low levels of testosterone in males.

Osteoporosis occurs in 15-66% of Haemochromatosis patients. Most have evidence of hypogonadism. Hypogonadism is a condition resulting from or characterised by abnormally decreased functional acitivity of the gonads.

To prevent Osteoporosis one is advised to have a well balanced diet with adequate protein, vitamin D and calcium. Smoking should be stopped and excessive alcohol and caffeine should be reduced. Thirty minutes daily of weight bearing exercise is recommended. Too little exercise may predispose to Osteoporosis as can overtraining.

Treatment options must be considered on an individual basis. It will depend on age group, gender, and medical history. The pharmacological treatments include HRT, Biophosphonates, Actonel, Bon Viva, Pamidronate and Fosomax.

For more information, contact Irish Osteoporosis Society,
33 Pearse Street, Dublin 2
Tel : 016774267
Email: info@irishosteoporosis.ie

OLIVIA'S STORY

I moved to Spain in early 2003. In January 2005 a routine health check under my company's health benefits scheme demonstrated "irregularities" in my blood and advised a visit to my GP for clarification. A further blood test by the GP showed a ferritin level of 664ng/ml which prompted the GP to do more tests. Two weeks later I had a diagnosis of Haemochromatosis . I had never heard of this condition, but on discussing it with my elder sister, I discovered that my father had been diagnosed with it 4 months before he died in 1997. However, this was not an issue at the time of his death as he was dying from lung cancer and multiple secondaries. His doctors gave the family advice on palliative treatment for the cancer but never mentioned or discussed Haemochromatosis or its hereditary nature. I had been feeling well for my 41 years prior to this diagnosis and received quite a shock to be told that I had a problem that required hospital treatment.

At the time of diagnosis I was using private health care even though I had access to the Spanish health system as I am fully resident and employed in this country. When I realised that the treatment would be ongoing I registered with the public health system. My treatment required a blood test, followed by a consultation and a venesection once a month at a haematology department in a local public hospital, which necessitated a half day's leave from work. The treatment was excellent and, to my surprise, the haematologist I was under in the public system was the same doctor who had previously seen me at the private hospital. I saw the same consultant and many of the same nurses throughout my venesection treatment which gave me great reassurance. I am now over two years since diagnosis and my ferritin level is within the normal range at 150ng/ml.

At initial diagnosis the haematologist encouraged me to advise my 3 siblings to be tested, which I did. As a result of their initial consultation, my 2 elder brothers were informed they were carriers and my elder sister had the condition. However, my eldest brother has been recently told by his GP that he has Haemochromatosis and that he is one of the few people who fall into the category of those whom are classed as carriers but also have the condition. As a result of this, he is currently having weekly venesections to reduce his ferritin level which was 1500ng/ml but has now reduced to 950ng/ml. My elder sister resides in the UK and her initial serum ferritin level of 436ng/ml is now down to 20ng/ml following twenty-five weekly venesections. She is currently on a three monthly programme of venesection. I find it somewhat confusing that the target ferritin level in my sister's case was 50ng/ml when the acceptable target here in Spain is 150ng/ml.

"I had been feeling well for my 41 years prior to this diagnosis and received quite a shock to be told that I had a problem that required hospital treatment."

I have now come to terms with the diagnosis and feel exceptionally lucky that Hereditary Haemochromatosis was detected prior to my feeling any adverse health effects. Compared with other mid-life health problems, regular venesection is a relatively easy treatment to ensure continuing good quality of life.

The IHA would like to thank Olivia for sharing her interesting story with us and for coming to Ireland especially for the AGM

SUCCESS OF MINI MARATHON

Despite the rain the women's mini-marathon was a great success. Several members and their friends participated and others who were not able to take part contributed generously. Members travelled up from Kerry, Kildare, Limerick, Mullingar, and Roscommon and of course Dublin was very well represented!

Back row from left: Ann, Margaret, Noreen, Ellen, Shelia, Una Front row from left: Kay, Michelle, Eavan, Leonora

IRELAND'S FIRST HAEMOCHROMATOSIS BLOOD DONATIONS

Blood taken from Haemochromatosis patients can now be donated to those in need. Julie-Anne Barnes reports in *the Irish Medical News* 02/07/2007

'The first blood donation from Haemochromatosis patients in Ireland has taken place at the Irish Blood Transfusion Service's blood donation clinic in Stillorgan, Dublin, marking the beginning of a year long pilot study. The landmark study is being led by Dr Brigid Gallagher, Medical Officer with the IBTS and Haemochromatosis Project Medical Officer.

Speaking to the *Irish Medical News* on the first day of the project, Dr Gallagher said some 25,000 units of blood are discarded every year from patients with Haemochromatosis.

The initial difficulty in taking Haemochromatosis blood, she explained, was the IBTS had never knowingly bled donors whose blood was going to be rendered medically unusable.

Because our guidelines are so strict it didn't seem it was ever going to be able to happen here. The donation has to be 100 per cent altruistic and because in some way there would be a benefit to these patients being blood donors, that was the stumbling block. These donors have seen their blood discarded and they are now making an extra journey to come to the clinic, there's no financial benefit and we are taking patients that are getting treatment free of charge, she said. If the pilot is successful it could see the IBTS increase donor numbers through Haemochromatosis patients and recover some of the loss of donors through the stringent guide lines in place, such as not being able to donate if you have lived in the UK for a cumulative period of 12 months between 1980 and 1996.

For now the clinic will open from 9am to 2pm on Fridays and a full clinic would mean 20 donors in attendance, but for the initial few weeks around six donors will be taken. All patients, to date, are being referred from St James's Hospital, Dublin.

Dr Gallagher said it is a great opportunity for the Hameochromatosis patients' blood to be used for transfusion purposes and she said the desire is strong amongst donors. In addition, Dr Gallagher said she will be approaching consultant hepatologists and gastroenterologists to make them aware of the pilot programme and recruit additional donors.

Haemochromatosis patients who have completed their depletion therapy and are on maintenance therapeutic venesections are eligible to donate as well as Haemochromatosis patients who can be:

- Up to the age of 70;
- Non-insulin dependent diabetes patients who are taking oralhypoglycaemics;
- Patients with hypertension but who are well controlled on oral medication;

The rationale, explains Dr Gallagher, is that these individuals are people who have tolerated the procedure of donating blood once a week.

The pilot study began on February 19 this year and work began on implementing the standard operating procedures in place. Once a patient has been referred to the Stillorgan clinic, they will have their blood taken for the year of the pilot study and will be looked after completely. Even a HH patient who has to be deferred if, for example, they have travelled to a malarial area ,the IBTS can take their blood and it will be discarded.

The same guidelines that are in place in St James's will be applied in the IBTS's clinic. A donor must have a ferretin level greater than 80ng/ml for a donation to be taken.

The study ends next February with the intention of extending the programme to other clinics pending approval for such a move.

Dr Gallagher has expressed her gratitude to Ms Liz Ellis, Clinical Nurse Specialist at St James's Hospital who has flagged the programme with patients; Dr Suzanne Norris, St James's Hospital; quality assurance, IT, and Quality Control Personnel with the IBTS; and Mr Sean O'Broin, Principal Biochemist, Nutrition Laboratory, St James's Hospital.

The Irish Haemochromatosis Society has expressed delight at the pilot programme. Ms Margaret Mullet, spokesperson for the Association said the IHA would like if the programme were extended to other parts of the country.

EUROPEAN FEDERATION OF ASSOCIATIONS FOR PATIENTS WITH HAEMOCHROMATOSIS (EFAPH)

The third Federation meeting will take place in London in September. The meeting will be attended by Fran Mullaney and Margaret Mullett. Details of progress will be reported in the next newsletter.

INFORMATION MEETINGS

This year the IHA hope to arrange a series of information meetings throughout the country. Details will be posted on the website. The possible venues are Cork, Galway, Monaghan, Dublin, Letterkenny and Waterford.

MID-WESTERN HAEMOCHROMATOSIS SUPPORT GROUP

Please contact Denise Mc Auliffe at 087 8298461 for information on future meetings. Currently patients are experiencing difficulty in accessing the nurse led venesection clinic at the Laboratory in Dooradoyle.The HSE is reviewing activity to see if improvements on this can be made. In the meantime, new and existing Haemochromotosis patients can be referred to the medical day unit or to any of the consultant physician clinics at Dooradoyle and are seen without delay. Venesection services are also provided at Ennis and Nenagh general hospitals.